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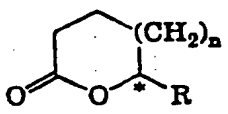
(54) Title: OPTICALLY ACTIVE LACTONES



(I)

(57) Abstract

The present invention relates primarily to the field of optically active lactones of formula (I) as defined below. The invention relates also to the utilisation of compounds of formula (I) so obtained as perfuming or flavoring ingredients. The process for producing the individual optically active lactones of formula (I), wherein the asterisk indicates a chirality center, n stands for zero or 1, R represents a C_5- or C_6-alkyl radical, which optionally may contain an additional double bond of either Z- or E-configuration, such additional bond being compulsory in case of n = 0, comprises the stereoselective enzymatic hydrolysis of the ester bond of the corresponding racemates in the presence of an esterase, recovering the enzyme-spared isomer, and, if desired, subjecting the hydrolysed isomer to lactonisation, provided the enzymatic hydrolysis is carried out in the presence of potassium ions in case of n = 1.

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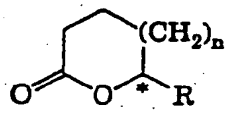
OPTICALLY ACTIVE LACTONES

The present invention relates primarily to the field of optically active lactones of formula I



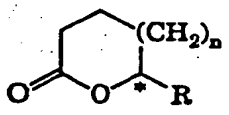
I

as defined below.

More exactly, the present invention provides an enzymatic process for the preparation of the compounds of formula I, which are strongly enriched in either the R- or the S-enantiomer, i.e. exhibiting optical purities of at least 50% ee.

The invention relates also to the utilization of compounds of formula I so obtained as perfuming or flavoring ingredients.

The process for producing the individual optically active lactones of formula I



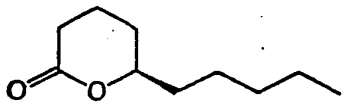
I

wherein the asterisk indicates a chirality center, n stands for zero or 1, R represents a C_5- or C_6-alkyl radical, which optionally may contain an additional double bond of either Z- or E-configuration, such additional bond being compulsory in case of n = 0, comprises the stereoselective enzymatic hydrolysis of the ester bond of the corresponding racemates in the presence

of an esterase, recovering the enzyme - spared isomer, and, if desired, subjecting the hydrolysed isomer to lactonisation,provided the enzymatic hydrolysis is carried out in the presence of potassium ions in case of n = 1.

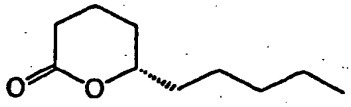
In the following table, the material products are depicted.

Table 1



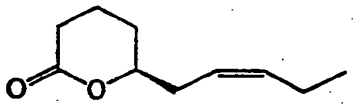
(+) - (R)

δ-delactone



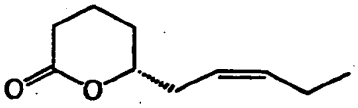
(-) - (S)

2a 2b



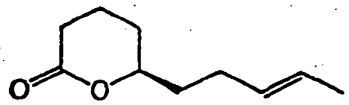
(+) - (S)

δ-jasmine lactone



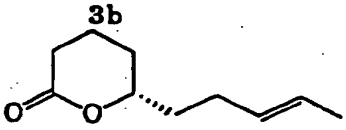
(-) - (R)

3a 3b



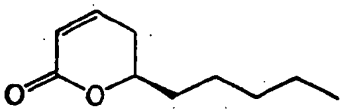
(+) - (S)

Jasmolactone



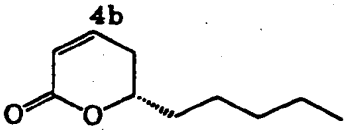
(-) - (R)

4a 4b



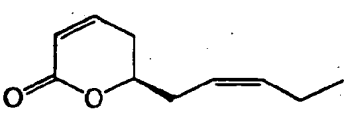
(-) - (R)

massoialactone



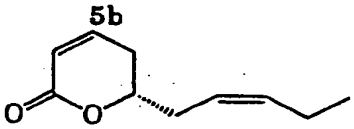
(+) - (S)

5a 5b



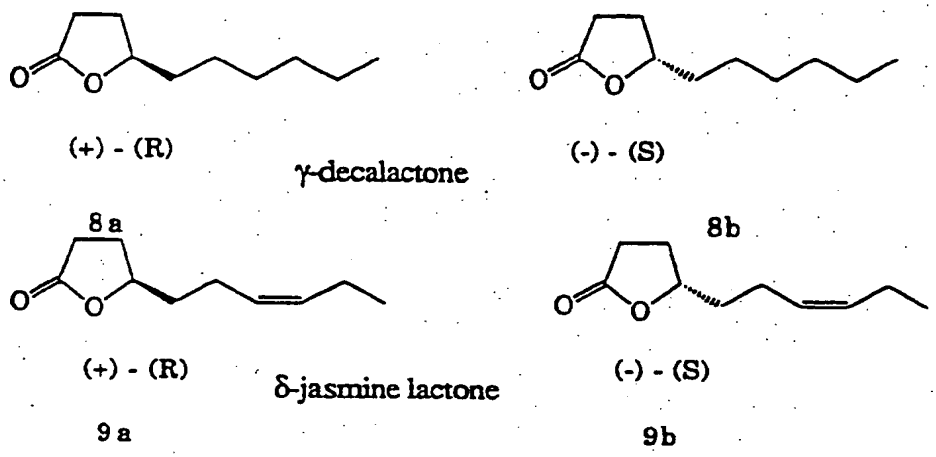
(-) - (R)

tuberolactone



(+) - (S)

6a 6b



Except for Jasmolactone (a synthetically prepared racemic lactone), all lactones mentioned in this context are known to occur naturally in either the R- and/or the S-configurated form.

For instance, (-)-(R)-δ-jasmine lactone 3b is found in jasmine oil [Winter M. et al., Helv. Chim. Acta. 45, 1250, 1962], whereas its (+)-(S) counterpart 3a is found in tuberose oil [Kaiser R., and Lamparsky D., Tetrahedron Lett. 20, 1659, 1976] together with (-)-(R)-tuberolactone 6a, (-)-(R)-massoïalactone 5a, and (+)-(R)-δ-decalactone 2a.

γ-Jasmine lactone (Z-dec-7-en-4-olide) of unspecified absolute configuration was found in jasmine oil [Stoffelsma J., Sipma G., Brouwer H., and Cohen A.M., Joint symposium on recent advances in perfumery, 1973, British Soc. of Perfumers; cited by Garnero J., Joulain D., and Buil P., Riv. Ital. EPPOS. 62 (1),8, 1980].

The natural occurrence of (+)-(S)-tuberolactone 6b and (+)-(S)-massoïalactone 5b has not been described in the literature. Actually, more and more examples become known, where the two enantiomeric forms of chiral compounds exhibit different organoleptic properties [for a recent review see Pickenhagen W., in Flavor chemistry,

Trends and developments, Teranishi R., Buttery R.G., and Shahidi F., Eds., ACS Symposium series 388, American Chemical Society, 1989, Washington DC., 151157].

Regarding γ-lactones, only a few publications compare the sensory characteristics of enantiomers : the enantiomers of 4-alkyl-substituted-γ-lactones were reported to exhibit distinct differences in odour quality as well as in odour and taste intensity (the (+)-(R)-antipodes being more pleasant and more intense than the (-)-(S)-antipodes) [Mosandl A., and Günther C., J. Agric. Food Chem. 37,413, 1989]. Not in line with the above made observations and also with the present results was a later published report where the odour of the (S)-enantiomer of (Z)-6-γ-dodeceno-lactone was described as more intense than that of the (R)-form, but no sensory difference was found with regard to the odour quality.
[Guichard E., Mosandl A., Hollnagel A., Latrasse A., and Henry R., Z. Lebensm. Unters. Forsch. 193,26, 1991].

Regarding δ-lactones previous publications state that the odour and/or the flavour of both enantiomers of δ-decalactone are identical [Tuynenburg Muys G., Van der Ven B., and De Jonge A.P., Nature, 194, 995, 1962] or only slightly distinct [Mosandl A., and Gessner M., Z. Lebensm Unters. Forsch. 187, 40, 1988]. This is in contradiction with the present results.

The enzymatic resolution of racemic lactones has been reported : racemic γ-lactones were resolved by porcine pancreatic lipase in 10% $CaCl_2$ (e.g. e.e. = 68% for γ-nonalactone), whereas racemic δ-decalactone - as a lactone with a saturated side chain - was resolved by use of horse liver esterase in sodium phosphate buffer (e.e. = 80%) [Blanco L., Guibé - Jampel E., and Rousseau G., Tetrahedron Lett. 29 (16), 1915, 1988]. In the latter case

the described resolution is very slow and produces decalactones with moderate enantiomeric excesses only.

Except for δ-decalactone, the enzymatic resolution of all other lactones investigated in the course of this work has never been described so far.

Both optically active forms (optical purities of at least 50% ee) of δ-decalactone, δ-jasmine-lactone, γ-jasmine lactone and Jasmolactone were prepared via enzymatic resolution (stereoselective hydrolysis of the internal ester bond) and their organoleptic properties were characterized. Alternatively both optically active forms of massoïalactone and tuberolactone were obtained by chemical transformation of the corresponding optically active δ-decalactones and δ-jasmine lactones.

For each lactone investigated, the organoleptic evaluation of the two optically active forms revealed, that they were unambiguously considerably different from each other and also from the racemate ; in addition the more a mixture of antipodes was enriched in a given enantiomer, the more the enantiomer-specific olfactive impact was exalted, and the more the racemate-specific note was vanishing. Finally, it is the contribution of a given enantiomer to the total scent of a perfume composition which is decisive, if such composition is compared to the corresponding the racemate of I containing composition. The same applies to the corresponding flavour compositions.

By a rule of thumb the enantiomers of (-)-5-alkylated-δ-decalactones are generally more intense and more fruity than the (+)-antipodes and therefore are more interesting for perfumery and flavour uses, e.g. (-)-(R)-δ-jasmine lactone 3b has a much more pronounced jasmine note than its (+)-(S)-antipode 3a. Likewise (+)-(R)-γ-jasmine lactone 9a is more intense and its flowery note is sweeter

than that of its (-)-(S)-antipode 9b, which in turn exhibits the coconut note found in the racemate.

With regard to the novel process it has been found, that changing the buffer from sodium phosphate (Blanco et al.) to potassium phosphate and introducing a double bond in the 5-alkyl side chain of δ-lactones dramatically increases the rate of the enzyme-mediated hydrolysis and simultaneously enhances significantly the stereoselectivities. Thus (-)-(R)-δ-jasmine lactone 3b was obtained within 2.3 hours (e.e. = 88%), while (-)-(S)-δ-decalactone 2b was obtained after two cycles of enzyme-catalyzed hydrolysis over a total period of 12 hours (e.e. = 82%) thereby using twice the amount of enzyme. This observed rate and stereoselectivity increase for side chain unsaturated δ-lactones is unexpected, since changing the spatial shape of an enzyme's substrate may drastically change the enzyme-substrate interaction or even cancel the enzyme's affinity for the substrate : e.g. racemic 4-methyl-4-hexyl-butyrolactone, massoïalactone and tuberolactone could not be resolved enzymatically under the usually applied conditions.

The principle of the enzymatic resolution of racemic lactones is as follows: the enzyme and the racemic lactone are treated, e.g. stirred in a buffered reaction medium, namely in a pH-range of ca. 6.8 to ca. 7.8, preferably at pH 7.2, whereupon stereoselective hydrolysis of the internal ester bond of one of the enantiomers occurs. The course of the reaction may be followed with the help of a pH-meter, and subsequent addition of alkali allows adjustment of the pH to the desired value and calculation of the conversion. When the conversion reaches 50%, the enzyme spared enantiomer is, conveniently, extracted with an organic solvent, whereas the enzyme-hydrolyzed enantiomer remains in the basic aqueous phase ; the latter

may then be retrieved by solvent extraction after acidification of the aqueous phase.

Suitable solvents for this process are hexane, cyclohexane, methyl-t-butyl ether, etc. preferably ethyl ether.

If desired, one or both of the separated enantiomers may preferably be subjected to a second cycle of enzyme-catalyzed hydrolysis in order to improve the enantiomeric excesses (e.g. for δ-decalactone and γ-jasmine lactone). However in the case of δ-jasmine lactone a single cycle allowed to reach a high enantiomeric excess (88%). For γ-jasmine-lactone are preferable used the buffer and enzymes described by Blanco et al., Tetrahedron Lett., 29 (16), 1915, 1988. (cf. scheme 2). For δ-lactones (cf. scheme 1) best results were obtained by using a potassium phosphate buffer, i.e. KH_2PO_4/K_2HPO_4 (range of pH : 6.8-7.8, preferably around 7.2). The rates of hydrolysis were markedly increased with this buffer, if compared to the sodium phosphate buffer described by Blanco et al.

The enzymes used were of esterase type, whereby said term also encompasses lipases, more specifically horse liver esterase, pig pancreatic lipase or pig liver esterase, preferably horse liver esterase. The alkali used for adjustment of the pH of the reaction medium were preferably either NaOH or KOH, preferably KOH if a potassium phosphate buffer was used. The hydrolysis reaction was preferably quenched by the addition of Celite and for the separation of the now Celite-bound enzyme centrifugation was preferred over filtration.

The solvents used for extraction were conveniently cyclic and aliphatic alkanes or ethers, preferably ethyl ether. After drying the combined organic phases over $MgSO_4$ and evaporation of the solvent, the crude lactones were

purified by flash chromatography on silica gel and/or by distillation at reduced pressure. The resulting enantiomerically enriched lactones were spectroscopically analyzed and organoleptically evaluated by a panel of perfumers. In contrast to the enzymatic resolution of δ-decalactone, as described by Blanco et al., which is, as pointed out above, inadequate for an industrial production (too slow, moderate enantiomeric excess), it was found that horse liver esterase shows a higher affinity for 5-alkenyl-δ-decalactones thereby inducing much higher enantioselectivities. Or in other words, it surprisingly was discovered, that 5-alkenyl-substituted δ-decalactones are much better substrates for this enzyme than δ-decalactone itself.

According to a further aspect of the invention enantiomerically enriched massoïalactone and tuberolactone can be prepared by converting optically active δ-decalactone and δ-jasmine lactone, respectively, to the corresponding allyl ß-oxoesters, which then in turn can be oxidatively decarboxylated using palladium acetate as catalyst (cf. Minami I., Nisar M., Yuhara M., Shimizu I., and Tsuji J., Synthesis, 992-998, 1987) Mercier C., Mignami G., Aufrand M. and Allmang G., Tetrahedron Letters, 1433-1436, 1991. The thus obtained optically active massoïalactone and tuberolactone were analytically and organoleptically characterized.

The convenient parameters for preparation of the allyl β-oxo-esters the are:

Solvent:	hexane, cyclohexane, tetrahydrofuran, MTBE, ethyl ether, etc., preferably cyclohexane.
Base:	sodium hydride, potassium hydride, potassium tert-butoxide, etc. preferably sodium hydride.
Temp.:	60-80°C, preferably reflux temperature of the solvent, e.g. ca. 81°C for cyclohexane.

Oxydative decarboxylation

Catalyst: a Palladium complex such as $Pd(OAc)_2$-CH_3CN, $Pd(OAc)_2$-PPh_3, $Pd(OAc)_2$-dppe, preferably $Pd(OAc)_2$-CH_3CN.

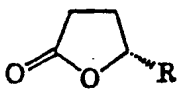
Solvent: nitriles or dinitriles, e.g. acetonitrile, benzonitrile, 1,6-dicyanohexane, etc., preferably acetonitrile.

Temp.: ca. 20 to ca. 80°C, preferably 80°C, i.e. reflux temperature of acetonitrile.

The mode of preparation for all lactones investigated is summarized in Schemes 1 and 2, their characteristics are compiled in Table 2 and their organoleptic properties are listed in Table 3.

The absolute configurations of the enantiomers of jasmolactone and γ-jasmine lactone were assessed via catalytic hydrogenation of their side chain double bonds and comparison of the optical rotation data of the resulting δ-decalactone and γ-decalactone, respectively, with literature values.

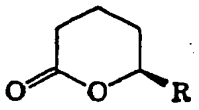
Surprisingly, a relationship was found, which consistently links absolute configuration with enzymatic selectivity, optical rotation and organoleptic impact. Thus, pig pancreatic lipase seems to selectively hydrolyse the (-) enantiomers of γ-lactones and all cases studied so far possess the below indicated configuration, independently of the nature of the 4-alkyl-substituent :



(-)-γ-lactone enantiomers

In addition the (+)-enantiomers of all γ-lactones investigated are more intense and exhibit a stronger sweet flowery note than their (-) antipodes.

Inversely, horse liver esterase seems to selectively hydrolyse the (+) enantiomers of δ-lactones (see Scheme 1 below) and all cases studied so far possess the below indicated configuration, independently of the nature of the 5-alkyl-substituent :



(+)-δ-lactone enantiomers

Here it is the (-)-enantiomers of the δ-lactones, which are more intense and more fruity than their (+)-counterparts ; they are more interesting for perfumery and flavor applications than their (+)-antipodes.

These organoleptic characteristics open new opportunities in the field of perfume and flavor compositions. Hence, by blending one of these optically active lactones (preferably a (+)-form for γ-lactones and a (-)-form for δ-lactones) with other odorants or flavourants, excellent perfume and flavor compositions can be obtained.

The art of preparing such odour or flavour compositions is well known to the skilled artisan.

Thus, the easy access to the individual isomers, i.e. the optically active lactones as enabled by the novel method opens new opportunitites if compared to the use of the corresponding racemates, in as fas as by blending one of these optically active lactones, preferably the (+) form for the γ-lactones and the (-) form for the δ-lactones, the final composition can be targeted: by adding the racemate, or the + form, or the - form to one and the same basic composition, the optimum formulation can easily be targeted. In the foreground of the interest are compounds 3b, 2b and 4b in this order of quoting them.

The thus obtained perfume compositions can be used in perfumes, soaps, shampoos, detergents, cosmetics, etc. and the flavor compositions in foodstuffs, drinks, etc.

EXAMPLES

General remarks

IR spectra were recorded on a NICOLET 510 FTIR spectrometer, absorption maxima are given in cm^{-1}.

^{1}H-NMR spectra (200 MHz) were recorded on a BRUKER AC 200 instrument using $CDCl_3$ as solvent. Chemical shifts are expressed in ppm (δ scale) ; abbreviations : s = singlet, d = doublet, t = triplet, m = multiplet.

Mass spectra were recorded on a FINNIGAN 4500 instrument (ionization voltage : 70 eV, acceleration voltage : 1500V, ion source temperature : 150°C).

Chiral Gas chromatography (CGC) was carried out on a PERKIN ELMER 8500 apparatus equipped with a FID-detector and a Lipodex E (MACHEREY-NAGEL) capillary column (25m x 0.25mm i.d., isotherm 140°C, carrier gas : 0.7ml/min.). Retention times (Rt) are given in minutes.

The potassium phosphate buffer ("KPO_4" buffer) was obtained by addition of 0.1M KH_2PO_4 to 0.1M K_2HPO_4 until the pH of 7.2 was reached.

In the following examples enzymatic powders and lactones were always added at once and without previous dilution.

All yields of the described enzymatic resolutions refer to initially engaged racemic material and therefore cannot exceed 50%.

The intended conversions of the enzymatic reactions were assessed from the amount of alkali necessary for the neutralization of the hydrolyzed lactone while maintaining the pH at 7.2.

For the organoleptic evaluations the remaining traces of solvent in case of nondistilled samples were removed by flushing with a nitrogen stream until the resminiscent solvent odour became undetectable.

EXAMPLE 1

Preparation of (-)-(S)-6-pentyl-tetrahydro-pyran-2-one 2b [(-)-(S)-δ- decalactone]

(-)-(S)-δ-decalactone 2b was obtained after two cycles of enzyme-catalyzed hydrolysis as described below via the enzyme-spared enantiomer (cf. Scheme 1).

A 500ml beaker equipped with a pH-meter and a magnetic stirrer was charged with 200ml of 0.1M "KPO_4" buffer (pH = 7.2) and 10 g of horse liver esterase (horse liver acetone powder, Sigma ref. L9627) and the pH of the resulting mixture was adjusted to 7.2 with 2M KOH. After the addition of 20g (117 mmol) of neat racemic δ-decalactone 1a (commercially available, Givaudan-Roure) the mixture was stirred at room temperature while maintaining the pH at 7.2 by controlled addition of 2M KOH (neutralization of liberated hydroxy-acid). After 6 hours the hydrolysis leveled off at a conversion of 37.5%. The pH was then adjusted to 9 with 2M KOH before the enzyme was inactivated by the addition of 10g of Celite (Celite 545, Prolabo, BP 389, 75526 Paris Cedex 11). Centrifugation left an aqueous supernatant, which was extracted with ethyl ether (3x100ml). The combined organic layers were washed with 9% aqueous $NaHCO_3$ (1x200ml), dried over $MgSO_4$ and concentrated in vacuo to furnish 10.9g (54.5%) of (-)-(S)-δ-decalactone, which according to chiral GC analysis

showed an enantiomer ratio of 2b/2a = 74/26 (ee = 48% namely (74-50) x 2).

In order to improve the optical purity of this partially resolved δ-decalactone a second enzymatic hydrolysis was carried out. Thus the above obtained 10.9g of (-)-(S)-δ-decalactone were added to a mixture of 100ml 0.1M "KPO_4" buffer and 5.5 g of horse liver esterase and stirred at room temperature while maintaining the pH at 7.2 by controlled addition of small amounts of 2M KOH. After 6 hours the hydrolysis leveled off at a conversion of 26%. Workup, carried out as described above, gave after distillation at reduced pressure (165°C/0.4mmHg) 5.5g (27.5%) of (-)-(S)-δ-decalactone 2b with an optical purity of 82% (GC purity 97%), e.e. = (82-50) 2 = 64%.

Chiral GC analysis : 2b/2a = 91/9 (e.e. = 82%) ; Rt of 2b = 16.05 ; Rt of 2a = 16.41.

$[\alpha]_D;^{28}$ = -36.3 (c = 2.29 in $CHCl_3$) (for the attribution of abs. configuration to 2a and 2b cf. Utaka M. et al., 1987, J. Org. Chem., 52, 4363-4368).

IR (cm^{-1}) : 930.5, 1036, 1052, 1167, 1186, 1244, 1342, 1379, 1465, 1737, 2862, 2933, 2955.

NMR (200 MHz, $CDCl_3$, ppm) : 0.85 (t, J = 6 Hz, 3H), 1.2-1.95 (m, 12H), 2.3-2.65 (m,2H), 4.15-4.35 (m, 1H).

GC-MS : 170(M^+,0), 152(2), 114(10), 99(100), 71(35), 55(33), 42(40).

The organoleptic properties of 2b are described in Table 3.

EXAMPLE 2

Preparation of (+)-(R)-6-pentyl-tetrahydro-pyran-2-one 2a [(+)-(R)-δ- decalactone]

(+)-(R)-δ-decalactone 2a was obtained after one cycle of enzyme-catalyzed hydrolysis via the enzyme hydrolyzed isomer (cf. Scheme 1).

The reaction was carried out as described in example 1, using 200ml of 0.1M "KPO_4" buffer, 9g of horse liver esterase and 18g (106 mmol) of racemic δ-decalactone 1a (commercially available, Givaudan-Roure). After 4 hours, the hydrolysis had reached a conversion of 36%, the pH was adjusted to 9 with 2M KOH and the enzyme inactivated by addition of 9g of Celite. Centrifugation and extraction of the aqueous supernatant with 3x100ml of ethyl ether (to remove 2b) was followed by acidification of the aqueous phase to pH < 2 using 10N HCl and reextraction with ethyl ether (3x100ml). The combined organic layers of this latter extraction were washed with water (200ml), dried over $MgSO_4$ and concentrated **in vacuo**. Purification of this crude lactone by flash chromatography over silica gel (200g, elution with hexane/ethyl acetate = 80/20) then afforded 3.3g (18.3%) of (+)-(R)-δ-decalactone 2a with an optical purity of 64% (GC purity ~100%).

Chiral GC analysis : 2a/2b = 82/18 (e.e. = 64%) ; Rt of 2a = 16.41 ; Rt of 2b = 16.05.
$[\alpha]_D^{30}$ = +31,6 (c = 1,81 in $CHCl_3$)
IR (cm^{-1}) : 931, 1036, 1052, 1168, 1187, 1245, 1342, 1379, 1465, 1736, 2861, 2933, 2955.
NMR (200 MHz, $CDCl_3$, ppm) : 0.85 (t, J = 6Hz, 3H), 1.2-1.95 (m, 12H), 2.25-2.65 (m, 2H), 4.15-4.35 (m, 1H).
GC-MS : 170(M^+,0), 152(2), 114(10), 99(100), 71(48), 55(39), 42(48).

The organoleptic properties of 2a are described in Table 3.

EXAMPLE 3

Preparation of (-)-(R)-6-(Z-pent-2-enyl)-tetrahydro-pyran-2-one 3b [(-)-(R)-δ-jasmine lactone]

(+)-(R)-δ-jasmine lactone 3b was obtained after one cycle of enzyme-catalyzed hydrolysis via the enzyme-spared isomer (cf. Scheme 1).

The reaction was carried out as described in example 1, using 200ml of 0.1M "KPO_4" buffer, 10g of horse liver esterase and 20g (119 mmol) of racemic δ-jasmine lactone 1b (cf. Utaka M. et al., J. Org. Chem., 51, 935-38, 1986 or refs cited therein). After 2h 20min. (4h 30min. if sodium phosphate buffer is used), when the hydrolysis had reached a conversion of 50%, extraction followed by distillation at reduced pressure (140°C/ 0.4mmHg) furnished 7.2g (36%) of (-)-(R)-δ-jasmine lactone 3b with an optical purity of 88% (GC purity 98%).

Chiral GC analysis : 3b/3a = 94/6 (e.e. = 88%) ; Rt of 3b = 18.00 ; Rt of 3a = 16.60.
$[\alpha]_D^{28} = -14.0$ (c = 2.0 in $CHCl_3$) (for the attribution of abs. configuration to 3a and 3b cf. Blaser F. et al., 1991, Helv. Chim. Acta, 74, 787-90).
IR (cm^{-1}) : 726, 933, 1047, 1132, 1159, 1183, 1242, 1340, 1362, 1383, 1444, 1463, 1737, 2877, 2935, 2962, 3012.
NMR (200 MHz, $CDCl_3$, ppm) : 0.95 (t, J = 7.5 Hz, 3H), 1.2-2.7 (m, 10H) 4.2-4.35 (m, 1H), 5.2-5.6 (m, 2H)
GC-MS : 168(M^+,6), 150(6), 108(10), 99(100), 81(10), 71(78), 55(51), 41(39).

The organoleptic properties of 3b and 3a are described in Table 3.

EXAMPLE 4

Preparation of (-)-(R)-6-(E-pent-3-enyl)-tetrahydro-pyran-2-one 4b [(-)-(R)-jasmolactone]

(-)-(R)-jasmolactone 4b was obtained after one cycle of enzyme catalyzed hydrolysis via the enzyme-spared isomer (cf. Scheme 1) starting from racemic Jasmolactone 1c (commercially available) and following the procedure given in example 3. After 6h 20min. a conversion of 50% was reached. After workup the crude, enzyme-spared lactone was distilled at reduced pressure (160°C, 4mmHg) to afford

5.8g (29%) of (-)-(R)-jasmolactone 4b with an optical purity of 72% (GC purity 97%).

Chiral GC analysis : 4b/4a = 86/14 (e.e. = 72%) ; Rt of 4b = 16.70 ; Rt of 4a = 17.35.
$[\alpha]_D^{28}$ = - 46.3 (c = 2.01 in $CHCl_3$) (the abs. configuration was attributed by correlation with (-)-(S)-δ-decalactone after catalytic hydrogenation of the side chain double-bond).
IR (cm^{-1}) : 931, 968, 1045, 1181, 1242, 1333, 1343, 1376, 1445, 1736, 2856, 2885, 2922, 2940, 3018.
NMR (200 MHz, $CDCl_3$, ppm) : 1.4-2.7 (m, 13H), 4.2-4.35 (m, 1H), 5.25-5.6 (m, 2H)
GC-MS : 168(M^+,10), 150(18), 108(42), 93(17), 81(67), 68(70), 55(100), 41(63).

The organoleptic properties of 4b and 4a are described in Table 3.

EXAMPLE 5

Preparation of (+)-(S)-6-(Z-pent-2-enyl)-5,6-dihydro-2H-pyran-2-one 6b [(+)(S)-tuberolactone]

(+)-(S)-tuberolactone 6b was prepared by starting from (-)-(R)-δ-jasmine lactone 3b as described in example 3.
A 250ml round bottomed flask, equipped with a mechanical stirrer, a condenser, a thermometer and a dropping funnel was charged with 13.2g (93 mmol) of diallyl carbonate (Prolabo), 7.1g (148.5 mmol) of sodium hydride (50% w/w mineral oil dispersion washed with 3x30ml of cyclohexane) and 150ml of anhydrous cyclohexane. This mixture was heated to reflux (81°C) under nitrogen before a solution of 7.8g (46.4 mmol) of (-)-(R)-δ-jasmine lactone 3b in 20ml of cyclohexane was added dropwise during approximately 1 hour. After stirring the reaction mixture for an additional 2 hours it was cooled to room

temperature and neutralized with a solution of 8.8g (148.5 mmol) of acetic acid in 50ml of water.
After separation of the organic layer the aqueous phase was extracted with hexane (2x50ml). The combined organic layers were washed with water (1x100ml), dried over $MgSO_4$ and concentrated in vacuo to furnish the corresponding allyl ß-oxo-ester (cf. Scheme 1), which was contaminated by excess diallyl carbonate. Purification by flash chromatography on silica gel (100g, elution with hexane/ethyl acetate 95/5 v/v) then gave 4.4g (37%) of allyl ß-oxo-ester (4.4g) which was oxidatively decarboxylated as described in the following.
A 50ml round bottomed flask equipped with a magnetic stirrer, a condenser and a thermometer was charged with 4.4g (17.4 mmol) of allyl ß-oxoester, 131mg (0.59 mmol) of palladium acetate (Aldrich) and 30ml of acetonitrile and the mixture was stirred at reflux and under argon for 3.5 hours. After cooling to room temperature and filtration on a cotton pad the reaction mixture was concentrated. GC analysis of the crude product indicated a tuberolactone/ℓ-jasmine lactone ratio of 60/40 thereby indicating that non-oxydative decarboxylation is equally taking place under these reaction conditions. Purification by flash chromatography on silica gel (100g, elution with hexane/diisopropylether = 80/20 v/v) yielded 0.8g (5%) of (+)-(S)-tuberolactone 6b with an optical purity of 96% (GC purity 91%).

Chiral GC analysis : 6b/6a = 98/2 (e.e. = 96%) ; Rt of 6b = 19.11 ; Rt of 6a = 17.90.
$[\alpha]_D^{27}$ = +127 (c = 0.77 in $CHCl_3$) (for the attribution of abs. configuration to 6b and 6a cf. Kaiser R. and Lamparsky D., 1976, Tetrahedron Lett. 20, 1659-60).
IR (cm^{-1}) : 815, 1035, 1050, 1069, 1152, 1248, 1387, 1724, 2876, 2935, 2964

NMR (200 MHz, $CDCl_3$, ppm) : 0.95 (t, J = 7.5 Hz, 3H), 1.2-2.65 (m, 6H), 4.3-4.55 (m, 1H), 5.25-5.65 (m, 2H), 5.95-6.05 (m, J = 5Hz, 1H), 6.8-6.9 (m, J = 5Hz, 1H)
GC-MS : 166(M^+,0), 121(5), 97(100), 81(20), 69(29), 41(30).

The organoleptic properties of 6b and 6a are described in Table 3.

EXAMPLE 6

Preparation of (+)-(S)-6-pentyl-5,6-dihydro-2H-pyran-2-one 5b [(+)-(S)-massoïalactone]

(+)-(S)-massoïalactone 5b was prepared by starting from (-)-(S)-δ-decalactone 2b (3.4g, 20 mmol), which was obtained as described in example 1, and by following the procedure given for (+)-(S)-tuberolactone 6b (example 5).
In this way 0.32g (9.5%) of (+)-(S)-massoïalactone 5b with an optical purity of 74% (GC purity 93%) were obtained.

Chiral GC analysis : 5b/5a = 87/13 (e.e. = 74%) ; Rt of 5b = 18.14 ; Rt of 5a = 18.80.
$[\alpha]_D^{27}$ = + 61.8 (c = 0.52 in $CHCl_3$) (for the attribution of abs. configuration to 5b and 5a cf. Pirkle W.H. and Adams P.E., 1980, J. Org. Chem., 45, 4117-4121).
IR (cm^{-1}) : 816, 954, 1040, 1058, 1119, 1158, 1252, 1387, 1465, 1726, 2862, 2933, 2956
NMR (200 MHz, $CDCl_3$, ppm) : 0.9 (t, J = 7 Hz, 3 H), 1.2-2.0 (m, 8H), 2.2-2.4 (m, 2H), 4.3-4.5 (m, 1H), 5.95-6.05 (m, J = 10 Hz, 1H), 6.8-6.9 (m, J = 10 Hz, 1H)
GC-MS : 168(M^+,0), 108(6), 97(100), 81(3), 68(66), 55(6), 41(18).

The organoleptic properties of 5b and 5a are described in Table 3.

EXAMPLE 7

Preparation of (+)-(R)- 9a and (-)-(S)-5-(Z-hex-3-enyl)-tetrahydro-furan- 2-one 9b [(+)-(R)- and (-)-(S)-γ-jasmine lactone]

(+)-(R)- and (-)-(S)- γ-jasmine lactones were obtained after two cycles of enzyme-catalyzed hydrolysis in 10% $CaCl_2$ (cf. Scheme 2).

A 100ml beaker equipped with a magnetic stirrer and a pH meter was charged with 20ml of 10% $CaCl_2$ (w/v), whose pH had been adjusted to 7.2 with 2M NaOH. Then 1g of porcine pancreatic lipase (Sigma) and 1 g (5.9 mmol) of racemic γ-jasmine lactone 7b [prepared as described by Stoll M. and Bolle P., 1938, Helv. Chim. Acta, 21, 1547-1553] were added and the mixture stirred at room temperature while maintaining the pH at 7.2 by controlled addition of 2M NaOH (neutralization of liberated hydroxy- acid). After 5 hours the hydrolysis leveled off at a conversion of 30%. The pH was then adjusted to 9 with 2M NaOH before the enzyme was inactivated by the addition of 1g of Celite (Celite 545, Prolabo). Centrifugation left an aqueous supernatant, which was extracted with ethyl ether (4x50ml) before it was acidified to pH 2 with 10 N HCl. The combined organic layers were washed with 9% aqueous $NaHCO_3$ (1x100ml), dried over $MgSO_4$ and concentrated at reduced pressure (20 mbars) to furnish 660mg (66%) of crude (+)-(R)- -jasmine lactone which according to chiral GC analysis showed an enantiomer ratio of 9a/9b = 62/38 (e.e. = 24%). The above obtained acidified aqueous phase was reextracted with ethyl ether (3x50ml) and the combined organic layers were washed with water (1x100ml), dried over $MgSO_4$ and concentrated in vacuo to afford 230mg of (-)-(S)-γ-jasmine lactone, which according to chiral GC analysis showed an enantiomer ratio of 9b/9a = 85/15 (e.e. = 70%).

In order to improve both the optical purity of the previously obtained (+)-(R)-γ-jasmine lactone 9a and the

yield of (-)-(S)-γ-jasmine lactone 9b a second hydrolysis cycle was carried out. Accordingly the above obtained 660mg of (+)-(R)-γ-jasmine lactone 9a were added to a mixture of 8ml of 10% $CaCl_2$ (pH adjusted to 7.2) and 1g of porcine pancreatic lipase under stirring while maintaining the pH at 7.2 by controlled addition of 2M NaOH. After 5 hours, the hydrolysis leveled off at a conversion of 21%. Work-up was carried out as described for the first cycle. The thus obtained enzyme-spared enantiomer was purified by flash chromatography on silica gel (20g, elution with hexane/ethyl acetate = 90/10) to furnish 287mg (28%) of (+)-(R)-γ-jasmine lactone 9a with an optical purity of 60% (GC purity ~100%). The enzyme-hydrolyzed lactone isolated during this second cycle as described above was combined with the corresponding extract from the first cycle (230mg) and purified by flash-chromatography on silica gel (20g, elution with hexane/ethyl acetate = 90/10) to afford 277mg (27%) of (-)-(S)-γ-jasmine lactone 9b with an optical purity of 66% (GC purity 95%).

Chiral GC analysis :
(+)-(R)-γ-jasmine lactone : 9a/9b = 80/20 (e.e. = 60%)
(-)-(S)-γ-jasmine lactone : 9b/9a = 83/17 (e.e. = 66%)
Rt of 9a = 15.27 ; Rt of 9b = 15.75
$[\alpha]_D^{30}$ = + 36.5 (c = 1.75 in $CHCl_3$) for 9a
$[\alpha]_D^{30}$ = - 37.3 (c = 1.74 in $CHCl_3$) for 9b

The absolute configuration was assessed by catalytic hydrogenation of the double-bond and correlation of the optical rotation with data available in the literature [Thij L. et al., Recl. Trav. Chim. Pays-Bas, 105, 332-337, 1986].
The spectral data are identical for both enantiomers.
IR (cm^{-1}) : 905, 913, 970, 1025, 1047, 1068, 1123, 1181, 1220, 1356, 1460, 1776, 2874, 2935, 2963, 3007.

NMR (200MHz, $CDCl_3$, ppm) : 0.95 (t, J = 8 Hz, 3 H), 1.6-2.4 (m, 8 H), 2.4-2.6 (m, J = 8 Hz, 2 H), 4.45 - 4.55 (m, 1H), 5.2 - 5.5 (m, 2 H).
GC-MS : 168(M^+,0.5), 150(3), 139(0.5), 122(1), 108(8), 95(6), 85(25), 79(11), 68(100), 55(15), 41(25).

The organoleptic properties of 9a and 9b are described in Table 3.

EXAMPLE 8

Preparation of (+)-(R)- 8a and (-)-(S)-5-hexyl-tetrahydrofuran-2-one 8b
[(+)-(R)- and (-)-(S)-γ-decalactone]

(+)-(R)- and (-)-(S)-γ-decalactones were obtained starting from racemic γ-decalactone after two cycles of enzyme-catalyzed hydrolysis as described in example 7. After 24 hours of reaction the hydrolysis leveled off at a conversion of 21% for the first cycle and 15% for the second cycle. In this way 4.4g (22%) of (+)-(R)-γ-decalactone 8a (optical purity of 30%, GC purity 99%) and 3.2g (16%) of (-)-(S)-γ-decalactone 8b (optical purity of 18%, GC purity 99.5%) were obtained.

Chiral GC analysis :
(+)-(R)-γ-decalactone : 8a/8b = 65/35 (e.e. = 30%)
(-)-(S)-γ-decalactone : 8b/8a = 59/41 (e.e. = 18%)
Rt of 8a = 45.3 ; Rt of 8b = 45.8 (isotherm 130°C)
$[\alpha]_D^{30}$ = + 12.5 (c = 1.83 in $CHCl_3$) for 8a
$\alpha]_D^{30}$ = - 6.3 (c = 2.09 in $CHCl_3$) for 8b

The spectral data are identical for both enantiomers.
IR (cm^{-1}) : 913, 967, 1022, 1127, 1183, 1218, 1352, 1463, 1778, 2859, 2932, 2956.
NMR (200MHz, $CDCl_3$, ppm) : 0.85 (t, J = 7 Hz, 3 H), 1.2-2.0 (m, 10 H), 2.2-2.6 (m, 4 H), 4.35-4.55 (m, 1H).

GC-MS : 152(0.3), 141(0.1), 134(0.2), 128(8.5), 110(2), 100(4), 85(100), 81(1), 70(3), 55(6), 41(5.5).

The organoleptic properties of 8a and 8b are described in Table 3.

EXAMPLE 9

Fragrance compositions of the floral, fruity and peachy type were prepared according to the following scheme (the parts are by weight) :

	A	B
Isoamyl acetate	5.00	5.00
Benzaldehyde	2.00	2.00
Ethyl butyrate	5.00	5.00
Nectaryl (p-1-menthen-9-yl)-2-cyclopentanone)	350.00	350.00
γ-Undecalactone	400.00	400.00
Ethyl isovalerianate	4.00	4.00
Vanillin	94.00	94.00
(-)-(S)-δ-decalactone 2b *	140.00	
(+/-)-δ-decalactone (2a/2b)		140.00
	1000.00	1000.00

* as prepared in example 1

Fragrance evaluation carried out by a panel of experts clearly showed, that fragrance composition A containing optically active (-)-(S)-δ-decalactone 2b is considerably stronger and much more peachy with a sweeter and a more lactonic effect than fragrance B, which instead contains the corresponding racemate 2a/2b.

EXAMPLE 10

Fragrance compositions of a floral, jasmine like and fruity type were prepared according to the following scheme (parts by weight) :

	A	B
Isoamyl acetate	6.00	6.00
Benzyl acetate	65.00	65.00
α-Damascone	2.00	2.00
Ethyl methyl phenyl-glycidate (Aldehyde C16)	30.00	30.00
Hedione (Methyldihydrojasmonate)	38.00	38.00
Indole	10.00	10.00
Linalool synthetic	4.00	4.00
γ-Undecalactone	5.00	5.00
Undecavertol	10.00	10.00
(-)-(R)-δ-jasmine lactone 3b *	830.00	
(+/-)-δ-jasmine lactone (3a/3b)		830.00
	1000.00	1000.00

* as prepared in example 3

Fragrance evaluation carried out by a panel of experts clearly showed, that fragrance composition A containing optically active (-)-(R)-δ-jasmine lactone 3b has a clear-cut fruity, apricot, frangipane and dry fruit like odour with a much more characteristic jasmine note than fragrance B, which instead contains the corresponding racemate 3a/3b. Simultaneously the strength and intensity of the lactonic base note in composition A have also been clearly improved.

EXAMPLE 11

Fragrance compositions of a floral, tuberose type were prepared according to the following scheme (parts by weight) :

	A	B
Benzyl acetate	55.00	55.00
Benzyl alcohol	20.00	20.00
Amyl cinnamic aldehyde	15.00	15.00
Hexyl cinnamic aldehyde	150.00	150.00
Methyl anthranilate	15.00	15.00
Methyl benzoate	10.00	10.00
Hydroxycitronellal	10.00	10.00
Linalool synthetic	55.00	55.00
Methoxy phenyl butanone	15.00	15.00
Undecalactone	45.00	45.00
Prunolide (γ-Nonalactone)	20.00	20.00
Benzyl salicylate	500.00	500.00
Methyl salicylate	20.00	20.00
Ylang Ylang oil extra pure	10.00	10.00
(-)-(R)-jasmolactone 4b *	60.00	
Jasmolactone		60.00
	1000.00	1000.00

* as prepared in example 4

Fragrance evaluation carried out by a panel of experts clearly showed, that fragrance composition A containing optically active (-)-(R)-jasmolactone 4b exhibits a much stronger floral note with more freshness towards a lighter tuberose note than fragrance B, which instead contains the corresponding racemate 4a/4b.

EXAMPLE 12

Apricot flavours were prepared according to the following scheme (parts by weight) :

	A	B
Propylene glycol	890.90	890.90
Butyric acid	10.00	10.00
γ-Undecalactone	2.00	2.00
Benzaldehyde	3.00	3.00
Ethyl butyrate	3.00	3.00
Ethyl acetate	10.00	10.00
Isoamyl acetate	10.00	10.00
Hexyl acetate	1.00	1.00
Linalool (synthetic)	5.00	5.00
Ethyl propionate	10.00	10.00
Methyl-2-butyric acid	10.00	10.00
Hex-2-trans-enol	3.00	3.00
Hex-3-cis-enol/Leaf alcohol	2.00	2.00
Acetic acid	10.00	10.00
β-Damascone	0.10	0.10
Homo-furonol (2-ethyl-4-hydroxy-5-methyl-dihydrofuran-3(2H)-one) 20% PG	20.00	20.00
(-)-(S)-δ-decalactone 2b *	10.00	
(+/-)-δ-decalactone (2a/2b)		10.00
	1000.00	1000.00

* as prepared in example 1

Flavour evaluation carried out by a panel of experts clearly showed, that flavour A containing optically active (-)-(S)-δ-decalactone 2b is much more fruity, more complete and rounded off than flavour B, which instead contains the corresponding racemate 2a/2b.

EXAMPLE 13

Strawberry flavours were prepared according to the following scheme (parts by weight) :

	A	B
Vanillin	1.00	1.00
Propylene glycol	900.00	900.00
Ethyl capronate	3.00	3.00
Diacetyl	1.00	1.00
Ethyl butyrate	20.00	20.00
Ethyl acetate	20.00	20.00
Ethyl iso-valerianate	2.00	2.00
Methyl-2-butyric acid	3.00	3.00
Hex-3-cis-enol/Leaf alcohol	10.00	10.00
Homo-furonol 20% PG (propylene glycol)	35.00	35.00
(-)-(R)-δ-jasmine lactone 3b *	5.00	
(+/-)-δ-jasmine lactone (3a/3b)		5.00
	1000.00	1000.00

* as prepared in example 3

Flavour evaluation carried out by a panel of experts clearly showed, that flavour A containing optically active (-)-(R)-δ-jasmine lactone 3b is more fruity, more complete, rounded off and natural than flavour B, which instead contains the corresponding racemate 3a/3b.

Table 2 : Characteristics of lactones prepared according to Schemes 1 and 2

lactones	yield [a]	ratio of enantiomers	e.e. %	$[\alpha]_D$	abs. config. of major enantiomers
2a/2b	19	82/18	64	+ 31.6	R [2]
2b/2a	28	91/ 9	82	- 36.3	S [2]
3a/3b	29	82/18	64	+ 5.6	S [1]
3b/3a	36	94/ 6	88	- 14.0	R [1]
4a/4b	7	75/25	50	+ 40.1	S
4b/4a	29	86/14	72	- 46.3	R
5a/5b	5	86/14	72	- 81.2	R [3]
5b/5a	5	87/13	74	+ 61.8	S [3]
6a/6b	10	80/20	60	- 88.7	R [4]
6b/6a	5	98/ 2	96	+127.0	S
8a/8b	22	65/35	30	+ 12.5	R
8b/8a	16	59/41	18	- 6.3	S
9a/9b	28	80/20	60	+ 36.5	R
9b/9a	27	83/17	66	- 37.3	S

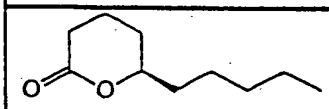
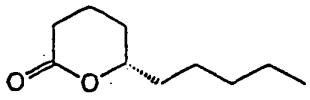
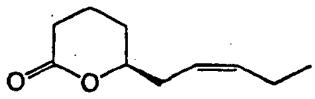
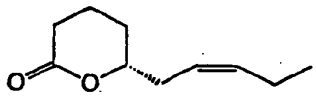
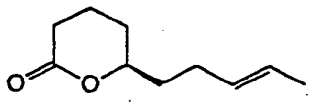
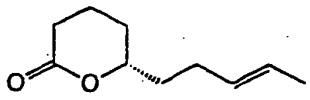
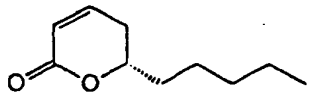
a) All yields given refer to initially used racemic material and therefore cannot exceed 50%.

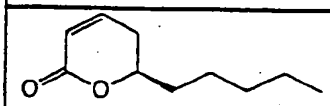
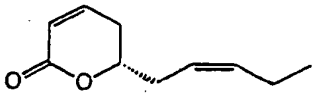
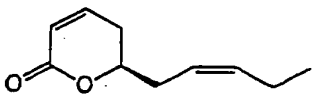
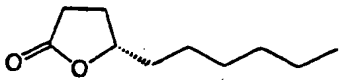
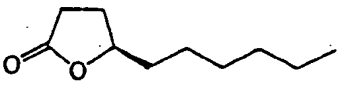
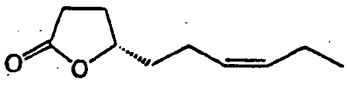
References :

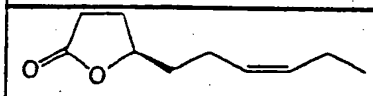
[1] Blaser F. et al. Helv. Chim. Acta. 74, 787-790, 1991.
[2] Utaka M. et al. J. Org. Chem. 52, 4363-4368, 1987.
[3] Pirkle W.H., and Adams P.E. J. Org. Chem. 45, 4117-4121 (1980).
[4] Kaiser R., and Lamparsky, D.; Tetrahedron Lett. 20, 1659-1660 (1976).

Table 3

Organoleptic properties of the optically active lactones of Schemes 1 & 2

Lactone	e.e. %	confg.	Organoleptic description
	64	(R) (+)	Top note: α-allyl-ionone; heavier, more lactonic and tuberose than racemate. Floral notes stronger than in S-(-)-enantiomer.
	82	(S) (-)	Fruity top note; heavier, milder and more coumarin but less tuberose than racemate. The more the sample is enriched in the R-(+)-enantiomer the more the floral notes are important; inversely, the more enriched in the S-(-)-enantiomer, the more the sample is intense and lactonic.
	64	(S) (+)	Fatty jasmin note; upon evaporation the sample gets more coconut and tuberose like. It is this enantiomer, which comes closest to the racemate: more rising and floral than the R-(-)-enantiomer.
	88	(R) (-)	Lactonic and proper jasmin note; jasmone and celeri note is equally present. Base note: fruity, lactonic and tuberose. The more the sample is enriched in the R-(-)-enantiomer, the more the base note is heavy, lactonic and after tuberose.
	50	(S) (+)	Exhibits a heavy woody coconut note with the spicy celery-jasmone aspect of the racemate; the base note is creamy tuberose like.
	72	(R) (-)	Exhibits a floral coconut note which is fresher and more rising than in the S-(+)-enantiomer; the fruity note is more marked than that of the racemate. Base note is coconut without the fatty aspect.
	74	(S) (+)	Fatty fruity (a bit tuberose like) top note, which is more intense than that of the (R)-(-) enantiomer. Upon evaporation the fatty aspects disappear in favor of a milky, coconut, tonka and a strong coumarine note.

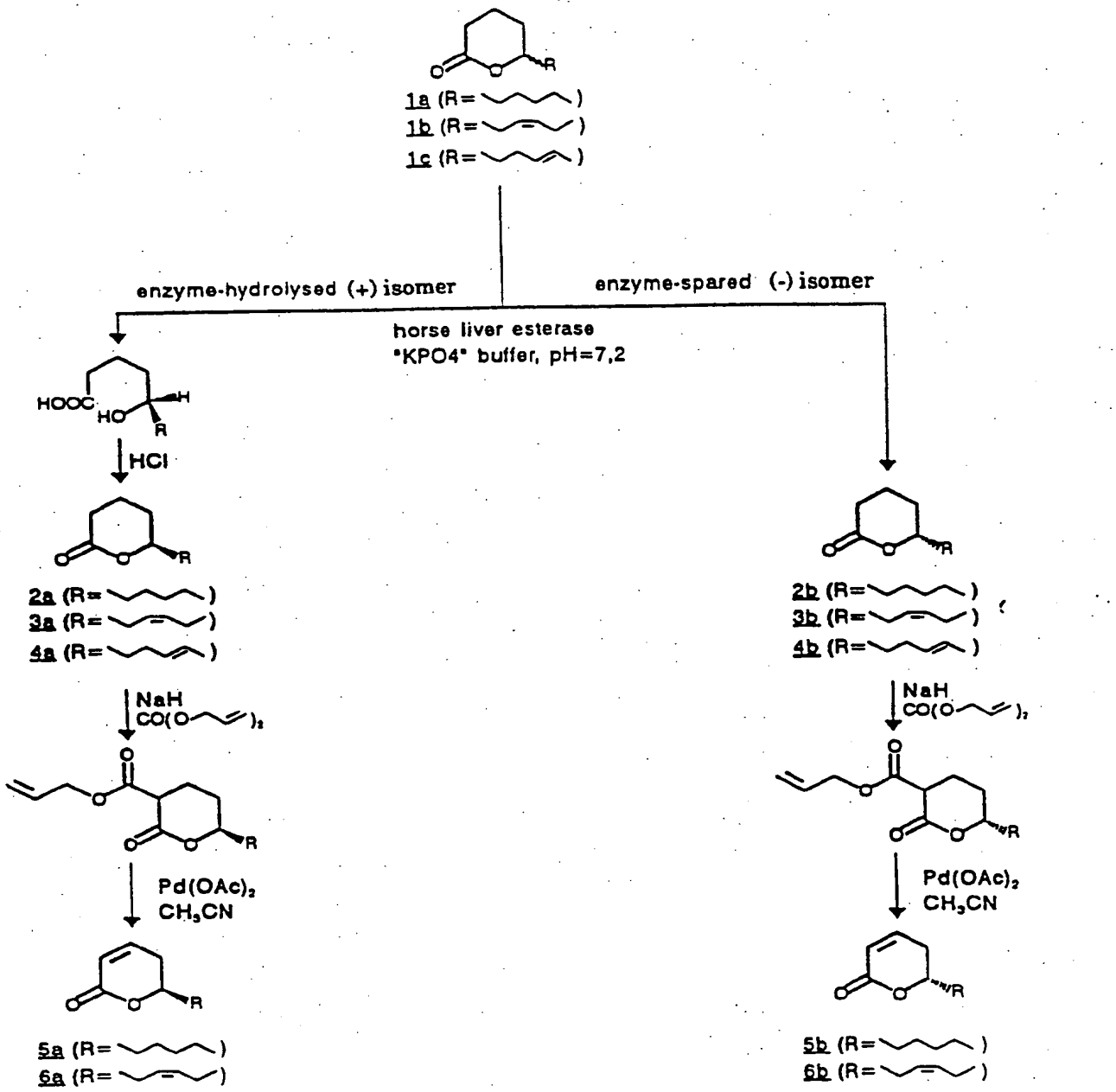
Lactone	e.e. %	confg.	Organoleptic description
	72	(R) (-)	Heavy tonka like top note and less fruity than (S)-(+)-enanticmer. Base note is strongly coconut like with fatty aspects. This enantiomer exhibits a more pleasant character with more volume than the racemate
	96	(S) (+)	Heavy fatty and less fruity top note. Upon evaporation becomes clearly lactonic, tuberose and tonka. In general much more volume than (R)-(-)-enantiomer. Less pleasant general floral note, but more voluminous than the racemate.
	60	(R) (-)	Fruity, coconut, tonka note with metallic and slightly fatty aspects. Base note, which is essentially tuberose lactonic, has less volume than (S)-(+)-enantiomer. In comparison to the racemate this enantiomer is more pleasant with regard to the tuberose note, but has less volume
	18	(S) (-)	Fruity, banana like, lactonic and jasmonic like floral top note. Base note is close to that of the racemate with more volume, less sweet and floral, but heavier and more lactonic.
	30	(R) (+)	Fatty, animalic top note. Upon evaporation clearly different from the racemate with regard to the acidic and animalic base notes; In particular suitable for flavours.
	66	(S) (-)	More heavy and lactonic, but less floral and mild than the R-(+)-enantiomer. Approaches rather a tuberose note, whereas the R-(+)-enantiomer tends towards jasmin. The S-(-)-enantiomer is organoleptically clearly less interesting than the R-(+)-enantiomer, but it is more tenacious and assures the coconut base of the racemate.

Lactone	e.e. %	confg.	Organoleptic description
	60	(R) (+)	Exhibits a mild floral, lactonic and coumarine-like note. It is more intense than the S-(-)-enantiomer. Each of these two enantiomers is very different from the racemate, which is strongly fatty.

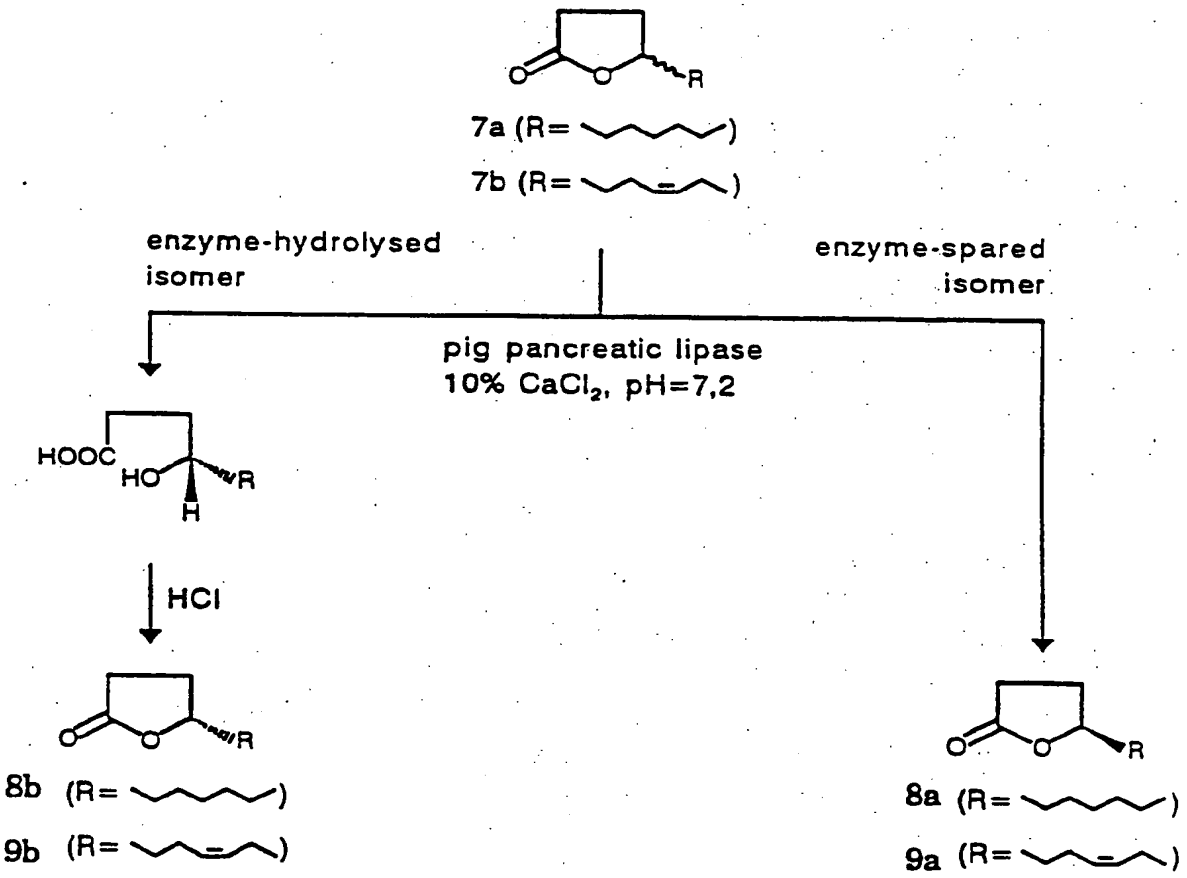
"Confg." = absolute configuration of the major enantiomer

e.e. = enantiomeric excess

SCHEME 1. Enzymatic resolution of racemic (50% +, 50% - enantiomer) δ-lactones and synthesis of optically active α,β-unsaturated lactones

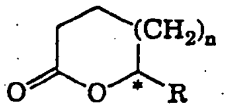


SCHEME 2. Enzymatic resolution of racemic δ-lactones



CLAIMS

1. A process for producing optically active lactones of formula



I

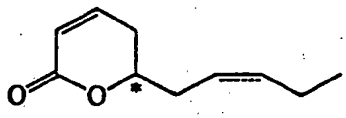
wherein the asterisk indicates a chirality center, n stands for zero or 1; R represents a C_5- or C_6-alkyl radical, which optionally may contain an additional double bond of either Z- or E-configuration, such additional bond being compulsory in case of n = 0, comprising the stereoselective enzymatic hydrolysis of the ester bond of the corresponding racemates in the presence of an esterase, recovering the enzyme - spared isomer, and, if desired, subjecting the hydrolysed isomer to lactonisation,
provided the enzymatic hydrolysis is carried out in the presence of potassium ions in case of n = 1.

2. A process according to claim 1, wherein the enzyme is an esterase, e.g. a lipase or a enzymatic extract containing the same, preferably horse liver esterase, pig pancreatic lipase or pig liver esterase.

3. A process according to claim 1 or 2, wherein in formula I n stands for 1 and an alkenyl side chain is a pentenyl group, preferably (Z)-2- pentenyl or (E)-3-pentenyl.

4. A process according to claim 1 or 2, wherein in formula I n stands for O and an alkenyl side chain is a hexenyl group, preferably (Z)-3- hexenyl.

5. A process for producing the optically active α,ß-unsaturated δ-decalactones of formula I'



I'

wherein the side chain may contain an additional double bond as indicated by the dotted line comprising the additional step of introducing a ring unsaturation into the saturated δ-lactones of formula I as prepared according to any one of claims 1 to 4.

6. A process according to claim 5 wherein the double bond is introduced according to Tsuji, e.g. via formation of the corresponding allyl ß-oxo esters of I followed by their palladium-catalyzed oxidative decarboxylation.

7. A perfume and/or flavour composition, containing at least a compound I of claim 1, prepared according to the process of any one of claims 1 to 6.

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INTERNATIONAL SEARCH REPORT

Inte. onal Application No
PCT/EP 93/02554

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 C07D309/30 C12P41/00 C11B9/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 C12P C07D C11B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TETRAHEDRON LETTERS. vol. 29, no. 16 , 1988 , OXFORD GB pages 1915 - 1918 L.BLANCO ET AL. 'Enzymatic resolution of racemic lactones.' cited in the application see the whole document ---	1
Y	HELVETICA CHIMICA ACTA. vol. 45, no. 4 , 1962 , BASEL CH pages 1250 - 1255 M.WINTER ET AL. 'Structure d'une lactone odorante présente dans l'essence de jasmin (Jasminum grandiflorum L.)' cited in the application see the whole document --- -/--	1

[X] Further documents are listed in the continuation of box C. [ ] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 January 1994	28 -01- 1994

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Delanghe, L

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TETRAHEDRON LETTERS. vol. 20 , 1976 , OXFORD GB pages 1659 - 1660 R.KAISER ET AL. 'Das Lacton der 5-Hydroxy-cis-2,cis-7-decadiensaüre und weitere Lactone aus dem Absolue der Blüten von Polianthes Tuberosa L.' cited in the application see the whole document	1
A	HELVETICA CHIMICA ACTA. vol. 45, no. 4 , 1962 , BASEL CH pages 1256 - 1260 E.DEMOLE ET AL. 'Synthèse du cis-(pentène-2-yl)-5-pentanolide-(5,1), composant odorant de l'essence de jasmin (Jasminum grandiflorum L.)' see the whole document	1
A	JOURNAL OF ORGANIC CHEMISTRY. vol. 55 , 1990 , EASTON US pages 3546 - 3552 A.GUTMAN ET AL. 'Lipase-catalyzed preparation of optically active gamma-butyrolactones in organic solvents.' see the whole document	1
A	CHEMICAL AND PHARMACEUTICAL BULLETIN. vol. 37, no. 5 , 1989 , TOKYO JP pages 1379 - 1381 H. SUEMUNE ET AL. 'Preparation of optically active gamma-hydroxyethyl alpha,beta-unsaturated gamma-lactone using an enzymatic procedure.' see the whole document	1

2